

Claims

What is claimed:

1. A method of identifying a peptide which modulates a biological process,
5 comprising:
 (a) contacting an organism, a cell or a tissue with a peptide library comprising a
 multiplicity of peptides, wherein said peptides are fragments of at least one gene product
 of an organism;
 (b) assessing the ability of said peptides to modulate the biological process in
10 said organism, said cell or said tissue; and
 (c) determining the amino acid sequence of at least one peptide shown in step (b)
 to modulate the biological process, thereby identifying the peptide as a modulator of the
 biological process.
- 15 2. The method of claim 1, wherein the biological process is apoptosis.
3. The method of claim 1, wherein the biological process is protein
 trafficking.
- 20 4. The method of claim 1, wherein the biological process is cell adhesion.
5. The method of claim 1, wherein the biological process is membrane
 transport.
- 25 6. The method of claim 1, wherein the biological process is cell motility.
7. The method of claim 1, wherein the biological process is cell
 differentiation.
- 30 8. The method of claim 1, wherein the biological process is the progression
 of a disease state.
9. The method of claim 1, wherein the organism is a pathogenic organism.
- 35 10. The method of claim 1, wherein the peptide library comprises a
 multiplicity of nested fragments of at least one gene product of the organism.

11. The method of claim 10, wherein the peptides each comprise 10 or more amino acid residues and the nesting overlap is 1 or more amino acid residues.

12. The method of claim 11, wherein the nesting overlap is from 1 to 5 amino acid residues.

13. The method of claim 1, wherein the peptide library comprises a multiplicity of fragments of at least two gene products of the organism.

10 14. The method of claim 1, wherein the peptide library comprises a multiplicity of fragments of gene products from at least one chromosome of the organism.

15 15. The method of claim 1, wherein the peptides each comprise about 50 or less amino acid residues.

16. The method of claim 1, wherein the peptides each comprise about 30 or less amino acid residues.

20 17. The method of claim 1, wherein the peptides each comprise about 20 or less amino acid residues.

18. The method of claim 1, wherein the peptides each comprise about 5 or less amino acid residues.

25 19. The method of claim 1, wherein said cell or said tissue is derived from said organism.

20. The method of claim 1, wherein said cell is a mammalian cell.

30 21. The method of claim 20, wherein said mammalian cell is a human cell.

22. The method of claim 1, wherein said cell is a yeast cell.

35 23. The method of claim 1, wherein said cell is an insect cell.

24. The method of claim 1, wherein said cell is a plant cell.

25. The method of claim 1, wherein the ability of said peptides to modulate the biological process in said organism, said cell or said tissue is assessed using immunohistochemistry.

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26. The method of claim 1, wherein the ability of said peptides to modulate the biological process in said organism, said cell or said tissue is assessed by monitoring a morphology change in said organism, said cell or said tissue.

10 27. The method of claim 1, wherein the ability of said peptides to modulate the biological process in said organism, said cell or said tissue is assessed by measuring a change in levels of signal transduction in said organism, said cell or said tissue.

15 28. The method of claim 27, wherein the change in levels of signal transduction is primarily mediated by a G protein coupled receptor.

20 29. The method of claim 1, wherein said peptides are fused to an additional amino acid sequence selected from the group consisting of a nuclear localization signal sequence, a membrane localization signal sequence, a farnesylation signal sequence, a transcriptional activation domain, and a transcriptional repression domain.

25 30. The method of claim 1, further comprising forming a second library comprising a multiplicity of peptide or non-peptide compounds designed based on the amino acid sequence identified in step (c) and selecting from the second library at least one peptide or non-peptide compound that modulates the biological process.

31. A method for identifying a peptide which modulates a biological process, comprising:

- (a) providing a library of expression vectors, each of said vectors comprising a nucleic acid sequence which encodes a member of a peptide library, wherein the peptide library comprises fragments of one or more proteins which are encoded by the genome of an organism;
- 30 (b) contacting a multiplicity of cells with the library of expression vectors under conditions suitable for transfection of the cells by the expression vectors and expression of the encoded peptide library within the cells;
- 35 (c) selecting a cell in which the biological process is modulated; and

(d) determining the nucleic acid sequence of step (a) in the cell of step (c), wherein the peptide which is encoded by the nucleic acid sequence is identified as a peptide which modulates the biological process.

5 32. The method of claim 31, wherein the library of expression vectors comprises viral vectors.

10 33. The method of claim 31, wherein each vector further includes a regulatory sequence which is operatively linked to the nucleic acid sequence which encodes a member of a peptide library.

34. The method of claim 31, where the peptide library comprises fragments of two or more proteins encoded by the genome of an organism.

15 35. The method of claim 34, wherein the peptide library comprises fragments of five or more proteins encoded by the genome of an organism.

36. The method of claim 35, wherein the peptide library comprises fragments of ten or more proteins encoded by the genome of an organism.

20 37. The method of claim 36, wherein the peptide library comprises fragments of fifteen or more proteins encoded by the genome of an organism.

38. The method of claim 37, wherein the peptide library comprises fragments of twenty or more proteins encoded by the genome of an organism.

39. The method of claim 38, wherein the peptide library comprises fragments of twenty-five or more proteins encoded by the genome of an organism

40. The method of claim 34, wherein the peptide library comprises fragments of each protein encoded by the genome of an organism.

41. The method of claim 31, wherein the cells are derived from the organism.

42. The method of claim 41, wherein the organism is a mammal, an avian animal, a bacterium, a fungus or a protozoan.

43. The method of claim 42, wherein the organism is a rodent or a primate.
44. The method of claim 42, wherein the organism is a human.
- 5 45. The method of claim 31, wherein the peptide library comprises fragments
of a protein encoded by the genome of a first organism and the cells are derived from a
second organism.
- 10 46. A method for identifying a peptide which modulates the infectivity of a
pathogenic organism, said method comprising:
(a) providing a library of expression vectors, each of said vectors comprising a
nucleic acid sequence which encodes a member of a peptide library, wherein the
peptide library comprises fragments of one or more proteins which are encoded by
the genome of the pathogenic organism;
- 15 (b) contacting a multiplicity of cells with the library of expression vectors under
conditions suitable for transfection of the cells by the expression vectors and
expression of the encoded peptide library within the cells;
(c) contacting the multiplicity of cells with the pathogenic organism;
(d) selecting a cell towards which the infectivity of the pathogenic organism is
modulated; and
- 20 (e) determining the nucleic acid sequence of step (a) in the cell of step (c), wherein
the peptide which is encoded by the nucleic acid sequence is identified as a
peptide which modulates the infectivity of the pathogenic organism.
- 25 47. The method of claim 46, wherein the multiplicity of cells is derived from
a mammal or an avian animal.
- 30 48. The method of claim 46, wherein the multiplicity of cells is derived from
a primate or a rodent.
49. The method of claim 46, wherein the cells are derived from a human.
50. The method of claim 46, wherein the library of expression vectors
comprises viral vectors.

51. The method of claim 46, wherein each vector further includes a regulatory sequence which is operatively linked to the nucleic acid sequence which encodes a member of a peptide library.

5 52. The method of claim 46, where the peptide library comprises fragments of two or more proteins encoded by the genome of the pathogenic organism.

53. The method of claim 52, wherein the peptide library comprises fragments of five or more proteins encoded by the genome of the pathogenic organism.

10 54. The method of claim 53, wherein the peptide library comprises fragments of ten or more proteins encoded by the genome of the pathogenic organism.

55. The method of claim 54, wherein the peptide library comprises fragments 15 of fifteen or more proteins encoded by the genome of the pathogenic organism.

56. The method of claim 46, wherein the pathogenic organism is a bacterium, a fungus, a protozoan or a virus.

20 57. A peptide which modulates a biological process identified according to the method of claim 1.

58. Use of a peptide which modulates a biological process identified 25 according to the method of claim 1, for the molecular modeling of a compound having similar binding characteristics as said peptide.

59. A pharmaceutical composition comprising a peptide which modulates a biological process identified according to the method of claim 1, and a pharmaceutically acceptable carrier.

30 60. A method for treating a disease or condition associated with an aberrant biological process in a subject, comprising administering to the subject a therapeutically effective amount of a peptide which modulates a biological process identified according to the method of claim 1.

35 61. The method of claim 60, wherein the disease or condition is HIV infection.

62. The method of claim 60, wherein the disease or condition is cancer.
63. A kit for identifying a peptide which modulates a biological process
5 comprising a peptide library comprising a multiplicity of peptides, wherein said peptides are fragments of at least one gene product of an organism and instructions for use.

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